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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,637	08/07/2001	Lawrence J. Marnett	N-6138 RSM	2070

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/27/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/923,637	Applicant(s) MARNETT ET AL.	
	Examiner MISOOK YU, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2002 and 17 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-86* is/are pending in the application.

4a) Of the above claim(s) *40-86* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group 1 corresponding to claims 1-39 in Paper No. 7 and further election of species, 6-keto-prostaglandin F1alpha-glycerol ester in Paper No. 11 is acknowledged.

Claims 40-86 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

Claims 1-39 will be examined to extent of the elected species and if the species is allowable, the search will expand to see if the generic claim is allowable.

Specification

The disclosure is objected to because it contains, for example at page 13, an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

fixed

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-39 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 13 recites "a 2-arachidonylglyderol (2-AG)" but it is not clear what the metes and bounds are for the phrase. The article "a" suggests that there might be more than one 2-arachidonylglycerol. It is not clear what is claimed for patent protection by the limitation.

still maintain ?

Claim 14 recites "a standard value" but it is not clear what the metes and bounds are for the limitation.

Claims 23 and 33 recite "a COX-2 selective substrate" but it is not clear what the metes and bounds are for the limitation. Does "a COX-2 selective substrate" mean all of the three known substrates? Note page 473, 1st column, 1st paragraph of Fritsche et al (2001, The Journal of Pharmacology and Experimental Therapeutics, Vol. 299, pages 468-467). The specification at page 10 line 9 to page 11 line 2 does not define what is claimed for patent protection by the limitation. Does it include yet unidentified substrate? What is the difference between the limitation "a COX-2 specific metabolite of a 2-arachidonylglyderol" in claim in 1 and 13 and the limitation "a COX-2 selective substrate"?

Claim 25 recites "relating the amount of the metabolite in the sample to the activity of the COX-2 enzyme in the subject" but it is not clear what the metes and bounds are for the limitation. The phrase does not tell what is being related between the detection of the metabolite to the status of COX-2 enzymatic activity.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim is interpreted as drawn to method of selectively detecting a COX-2 enzymatic activity by detecting COX-2 specific metabolite derived from 2-AG using an antibody. The specification does not teach any antibody specific for COX-2 specific metabolite derived from 2-AG but says at page 27-28 that monoclonal and polyclonal antibodies to PG-Gs or their metabolites can be made using the technology known in the art. Belvisi et al (1997, British Journal of Pharmacology 120 (5):p910-916) teach at page 911, 2nd column, 1st paragraph that making antibody to small organic molecules such as metabolites of COX-2 is known in the art but also teach the main problem of using an antibody to COX-2 antibody is cross-reactivity.

Since metabolites from 2-AG and arachidonic acid are similar in structures and sizes, for example, note that the difference between 6-keto prostaglandin F1alpha and 6-keto prostaglandin F1alpha ester is minor, it seems quite likely that an antibody to, lets say, 6-keto prostaglandin F1alpha ester might cross-react with 6-keto prostaglandin F1alpha; this would make selective detection of COX-2 activity difficult. Because of the limited guidance, lack of working examples, and unpredictability in the art, it is concluded that undue experimentation would be required to use the invention as claimed.

Claims 1-3, 5-16, 18-26, 28-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for HETE-G, PGE2-G, 6-keto prostaglandin F1alpha-G, does not reasonably provide enablement for any other metabolites. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims are drawn to method of detecting COX-2 specific metabolites. The specification teaches at Fig. 11 (MS data), Fig. 12 (reverse HPLC data), and page 34 line 23 that not all COX-2 specific metabolites are detected. LaPointe et al (Jan. 1998, Hypertension, Dallas, 31, 1 PART 2, p218-224) further teach at the abstract, and page 219 2nd column, 1st paragraph that not all COX-2 metabolites are stable enough to be detected. Considering the broad scope of the claims, unpredictability in the art, and the limited teachings of the specification, it is concluded that undue experimentation would be required to enable the full scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23-25 and 33 rejected under 35 U.S.C. 102(b) as being anticipated by Futaki et al (Dec. 1997, Inflammation Research 46: p496-502), LaPointe et al (Jan.

1998, Hypertension, Dallas, 31, 1 PART 2, p218-224), Hamiltin et al (Oct. 1997, British Journal of Pharmacology 122, PROC. SUPPL, p22P), Belvisi et al (1997, British Journal of Pharmacology 120, p910-916), or WO 98/50033 (11-12-1998).

The claims are interpreted as drawn to method of detecting COX-2 enzymatic activity by detecting a metabolite generated by a COX-2 enzyme.

Futaki et al teach a method of detecting COX-2 enzymatic activity by detecting 6-keto prostaglandin F1alpha and other metabolites at the abstract, at Materials and Method sections, Fig. 1 at page 498.

LaPointe et al also teach a method of detecting COX-2 enzymatic activity by detecting 6-keto prostaglandin F1alpha and other metabolites at the abstract, Methods section, and Fig. 1 at page 220.

Hamiltin et al also teach a method of detecting COX-2 enzymatic activity by detecting 6-keto prostaglandin F1alpha.

Belvisi et al (1997, British Journal of Pharmacology 120 (5):p910-916) also teach a method of detecting COX-2 enzymatic activity by detecting 6-keto prostaglandin F1alpha and other metabolites at the abstract, Methods section, Fig. 7.

WO 98/50033 (11-12-1998) also teaches at page 53-63 an assay to detect activity COX-2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kalgutkar et al (January 18, 2000, Proc. Natl. Sci. Acad. USA, Vol. 97, pages 925-930) as evidenced by page 33744, 2nd column, 2nd paragraph of Kozak et al (Oct. 27, 2000, J. Biol. Chem. Vol. 275, pages 33744-9) in view of Felder et al (1998, Annu. Rev.

Pharmacol. Toxicol. Vol. 38, pages 179-200) and further in view of WO 98/50033 (cited above).

The claims are interpreted as drawn to method of detecting COX-2 enzymatic activity by detecting various prostaglandin esters generated following COX-2 action on 2-AG.

Kalgutkar
~~Kozak et al~~ (January 18, 2000, Proc. Natl. Sci. Acad. USA, Vol. 97, pages 925-930) teach at page 925 that an assay capable of distinguishing COX-2 and COX-1 activities is valuable because it could be used to screen clinically useful COX-2 inhibitors and further teach at Table 1 and the paragraph bridging pages 926 and 927 that esterification of indomethacin, a COX-2 inhibitor results in highly selective COX-2 inhibition and also teach at the Materials and Methods section that COX-2 enzymatic activity could be detected by measured by detecting prostaglandin products generated following COX-2 action on arachidonic acid. WO 98/50033 teaches at the abstract that inhibition of COX-2 enzymatic activity selectively without simultaneously inhibiting COX-1 activity in vivo is desirable because COX-1 inhibition cause undesirable side effects in vivo and further teaches throughout the entire document that selectively measuring COX-2 activity is desirable to screen clinically useful drugs. Neither Kozak et al nor WO 98/50033 teaches 2-AG. However, Felder et al teach at Table 1 and Figure 3 at page 185 that that 2-AG, an esterificaton product of arachidonic acid is well known substance. Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to test if 2-AG, esterification product of arachidonic acid (arachidonic acid acts as a substrate for both COX-1 and COX-2) could act as a substrate for COX-2 only since esterification of indomethacin leads to highly selective COX-2 inhibition.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-

308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
November 22, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600